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Bioadhesiveness of thiolated pectin for buccal delivery of carbenoxolone sodium

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A R T I C L E I N F O

Article history:
Available online 25 November 2015

Keywords:
Thiolated pectin
Carbenoxolone sodium
Buccal disc

Pectin is a biopolymer that has numerous useful purposes in food and beverage industry, cosmetic products and pharmaceutical fields. One of the important properties of pectin is its bioadhesive properties. Native pectin provides fair bioadhesive properties that can be improved by modification of pectin structure. The immobilization of thiol groups on polymer can significantly improve the bioadhesive properties due to *in situ* cross-linking between thiol groups of polymer and mucin [1]. Recently, the dosage forms based on thiolated polymers such as microspheres, nanoparticles, gels, lipid formulations and matrix tablets have been developed for intraoral, peroral, ocular and vaginal drug delivery. Carbenoxolone sodium has been used clinically to treat gastric, peptic, esophageal, oral ulceration and inflammation. Electrolyte imbalance is a serious side effect of carbenoxolone when used systemically [2]. Therefore, the intraoral dosage form, i.e., buccal discs, was developed for local treatment of aphthous ulcer using thiolated pectin as bioadhesive polymer.

Two different pectins, that is, low methoxy (degree of esterification (DE) of 38%) and high methoxy (DE of 70%) pectins were used as starting materials for the synthesis of thiolated pectin. Briefly, the thiolated pectins were synthesized by esterification of pectin with thioglycolic acid (TGA) in the absence or presence of hydrochloric acid [3]. The reaction was performed by varying mole ratios of TGA to hydroxyl group of pectin. After synthesis, all samples were purified by dialysis method and then freeze-dried. Thiolated pectins were subjected to analysis by FTIR spectroscopy. Content of sulfhydryl group was determined by Ellman's reagent assay, using cysteine as a standard. Viscosity of thiolated pectin solution (about 0.6% w/w) was also determined. To prepare buccal discs, thiolated pectin was dissolved in distilled water, mixed with carbenoxolone sodium at a ratio of 1:4, poured to glass plate and dried at 50 °C. The dried samples were ground and compressed to discs. The adhesiveness of pectin discs was tested on porcine buccal mucosa using texture analyzer (TA.XT plus,

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Peer review under responsibility of Shenyang Pharmaceutical University.
http://dx.doi.org/10.1016/j.ajps.2015.11.095

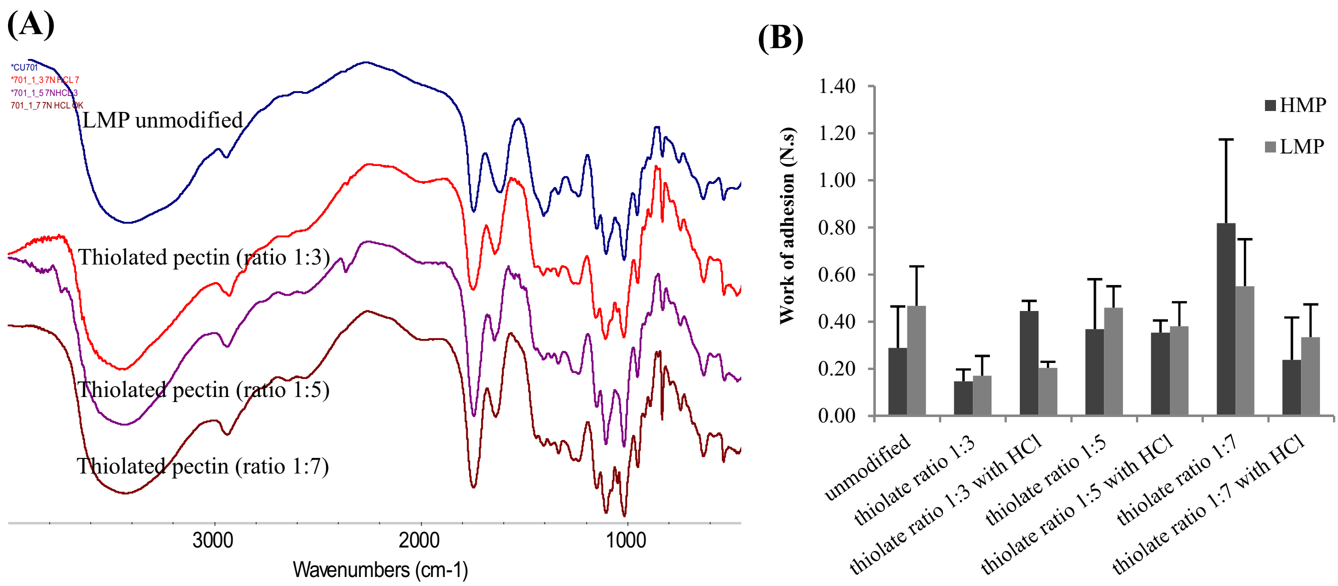

Fig. 1 – (A) FT-IR spectra of LMP pectin and thiolated pectins prepared at different mole ratios of TGA to hydroxyl group of pectin; and (B) work of adhesion of dried pectin discs (HMP and LMP) against porcine buccal tissue (n = 4–6).

Stable Micro Systems, UK), with 50-N load cell equipped with bioadhesive holder. The contact force and contact time were set at 0.05 N and 60 s, respectively. Two parameters derived from texture analysis, namely maximum detachment force (F_{max}) and work of adhesion (W_{ad}), were used as parameters for comparison of bioadhesive performance. The covalent bond between pectin and TGA was produced through hydroxyl group of galacturonic acid of pectin backbone and carboxyl group of TGA. From the FTIR spectra, when the amount of TGA increased, the intensity of carbonyl (C═O) of acid at 1650 cm^{-1} decreased but that of carbonyl of ester at 1750 cm^{-1} increased (Fig. 1A), suggesting the increase in esterification reaction. The content of sulfhydryl group, both in HMP and LMP, also increased when the amount of TGA was increased. The viscosity results showed a slightly difference between pectin and thiolated pectin. The bioadhesive properties of thiolated pectins on buccal tissue depended on mole ratios of TGA to hydroxyl group of pectin. W_{ad} of thiolated pectin prepared at mole ratio of 1:7 exhibited highest value (Fig. 1B), resulting from the highest content of sulfhydryl group.

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